Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L2	(alpha4 or 'alpha-4' or 'vla-4') same (herpes or arbovirus)	28	L2
L1	(alpha4 or 'alpha-4' or 'vla-4') and (herpes or arbovirus)	357	L1

END OF SEARCH HISTORY

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LIGHT set on as ' '
? begin 5,73,155,399
       20nov03 08:26:59 User208760 Session D2399.2
            $0.00    0.070 DialUnits File410
     $0.00  Estimated cost File410
     $0.01  TELNET
     $0.01  Estimated cost this search
     $0.32  Estimated total session cost   0.159 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2003/Nov W3
         (c) 2003 BIOSIS
*File   5: BIOSIS Previews has been reloaded with major enhancements.
See HELP NEWS005 for more information.
  File  73:EMBASE  1974-2003/Nov W3
         (c) 2003 Elsevier Science B.V.
  File 155:MEDLINE(R)  1966-2003/Nov W2
         (c) format only 2003 The Dialog Corp.
*File 155: On 13 November, Medline will temporarily stop updating with
Completed records. Please see HELP NEWS 154 for details.
  File 399:CA SEARCH(R)  1967-2003/UD=13921
         (c) 2003 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
Alert feature enhanced for multiple files, etc. See HELP ALERT.

      Set  Items  Description
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? s (vla(w)4) and (herpes or arbovirus)
            7256  VLA
         5848981  4
            4630  VLA(W)4
          138020  HERPES
           20535  ARBOVIRUS
      S1       3  (VLA(W)4) AND (HERPES OR ARBOVIRUS)
? rd s1
...completed examining records
      S2       3  RD S1 (unique items)
? t s2/7/all

 2/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

0010745663   BIOSIS NO.: 199799379723
Therapy with antibody against leukocyte integrin VLA-4 (CD49d)
  is effective and safe in virus-facilitated experimental allergic
  encephalomyelitis
AUTHOR: Soilu-Hanninen M (Reprint); Roytta M; Salmi A; Salonen R
AUTHOR ADDRESS: Dep. Virology, Univ. Turku, Kiinamyllynkatu 13, FIN-20520
  Turku, Finland**Finland
JOURNAL: Journal of Neuroimmunology  72 (1): p95-105 1997 1997
ISSN: 0165-5728
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Experimental allergic encephalomyelitis (EAE) is facilitated in
  resistant BALB/c mice by intraperitoneal infection with an avirulent
  Semliki Forest virus (SFV-A7). Viral infection increases the incidence of
  EAE from 15-30% to 60-90% and speeds up appearance of paralysis from 24
  to 14 days. In this paper, we describe treatment of virus-facilitated EAE
  with monoclonal antibodies (mAbs) against leukocyte and/or endothelial
  cell adhesion molecules. Therapy with mAb against ICAM-1 (intercellular
  adhesion molecule-1) had a modest effect, but caused hemorrhagic brain
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and spinal cord lesions. Therapy with mAb against Mac-1 (alpha-M beta-2-integrin) was well tolerated but had no effect. Therapy with mAb against **VLA-4** (alpha-4-beta-1-integrin) was safe, diminished both clinical and histopathological signs of EAE, decreased induction of VCAM-1 (vascular cell adhesion molecule-1) on brain vessels and diminished infiltration of **VLA-4**+ cells into the brain. The amount of viral antigen in the brain was riot altered. We conclude that facilitation of leukocyte entry into the brain is a major mechanism for viral facilitation of EAE in the BALB/c mouse, and that facilitation can be inhibited by anti-adhesion therapy. This may have implications for treatment of relapses triggered by viral infections in multiple sclerosis.

2/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010438569 BIOSIS NO.: 199699072629
Therapy with antibody against leukocyte integrin **VLA-4** is effective and safe in virus facilitated EAE
AUTHOR: Soilu-Hanninen Merja; Roytta Matias; Salmi Aimo; Salonen Reijo
AUTHOR ADDRESS: Dep. Virol., Univ. Turku, Kiinamyllynkatu 13, 20520 Turku, Finland**Finland
JOURNAL: Scandinavian Journal of Immunology 43 (6): p727 1996 1996
CONFERENCE/MEETING: XXVIIth Meeting of the Scandinavian Society for Immunology Turku, Finland May 24-27, 1996; 19960524
ISSN: 0300-9475
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

2/7/3 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

137154857 CA: 137(11)154857u PATENT
Preparation of nicotinamide biaryl derivatives as inhibitors of PDE4 isozymes
INVENTOR(AUTHOR): Chambers, Robert James; Magee, Thomas Victor; Marfat, Anthony
LOCATION: USA
ASSIGNEE: Pfizer Productors Inc.
PATENT: PCT International ; WO 200260875 A1 DATE: 20020808
APPLICATION: WO 2001IB2341 (20011206) *US PV265492 (20010131)
PAGES: 224 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07D-213/82A; C07D-405/12B; A61K-031/44B; A61P-011/06B; A61P-029/00B
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD ; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG
SECTION:
CA227016 Heterocyclic Compounds

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 s (vla(w)4) and (encephalitis)(10n)(viral or virus?)
           7256  VLA
        5848981  4
           4630  VLA(W)4
          59459  ENCEPHALITIS
         703314  VIRAL
        1711766  VIRUS?
          28499  ENCEPHALITIS(10N)(VIRAL OR VIRUS?)
      S3      13  (VLA(W)4) AND (ENCEPHALITIS)(10N)(VIRAL OR VIRUS?)
? rd s3
...completed examining records
      S4       6  RD S3 (unique items)
? t s4/3/all

 4/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

0010373776   BIOSIS NO.: 199699007836
Regulation of lymphocyte homing into the brain during viral
  encephalitis at various stages of infection
AUTHOR: Irani David N (Reprint); Griffin Diana E
AUTHOR ADDRESS: Dep. Neurol., Johns Hopkins Hosp., Meyer 6-181, 600 N.
  Wolfe St., Baltimore, MD 21287-7681, USA**USA
JOURNAL: Journal of Immunology  156 (10): p3850-3857 1996 1996
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English


 4/3/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

0009655216   BIOSIS NO.: 199598123049
Immunopathogenic role of T-cell subsets in Borna disease virus
  -induced progressive encephalitis
AUTHOR: Planz Oliver; Bilzer Thomas; Stitz Lothar (Reprint)
AUTHOR ADDRESS: Inst. Virol., Justus-Liebig-Univ., Frankfurter Str. 107,
  D-35392 Giessen, Germany**Germany
JOURNAL: Journal of Virology  69 (2): p896-903 1995 1995
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English


 4/3/3     (Item 3 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

0008960032   BIOSIS NO.: 199396124448
A model of human immunodeficiency virus encephalitis in SCID
  mice
AUTHOR: Tyor William R (Reprint); Power Christopher; Gendelman Howard E;
  Markham Richard B
AUTHOR ADDRESS: Dep. Neurol., Med. Univ. South Carolina, 171 Ashley Ave.,
  Charleston, SC 29425, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United
States of America  90 (18): p8658-8662 1993
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
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LANGUAGE: English

4/3/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05751151 EMBASE No: 1994154994
Monocyte adhesion to endothelium in Simian immunodeficiency **virus** -induced AIDS **encephalitis** is mediated by vascular cell adhesion molecule-1/alpha4beta1 integrin interactions
Sasseville V.G.; Newman W.; Brodie S.J.; Hesterberg P.; Pauley D.; Ringler D.J.
New England Reg. Primate Res. Center, Harvard Medical School, P.O. Box 9102,Southborough, MA 01772-9102 United States
American Journal of Pathology (AM. J. PATHOL.) (United States) 1994, 144/1 (27-40)
CODEN: AJPAA ISSN: 0002-9440
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

4/3/5 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11163639 98039725 PMID: 9372456
Semliki Forest virus infection leads to increased expression of adhesion molecules on splenic T-cells and on brain vascular endothelium.
Soilu-Hanninen M; Roytta M; Salmi A A; Salonen R
Turku Immunology Centre, University of Turku, Finland.
Journal of neurovirology (ENGLAND) Oct 1997, 3 (5) p350-60, ISSN 1355-0284 Journal Code: 9508123
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

4/3/6 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10241943 96043309 PMID: 7472530
[HIV and dementia: neuropathology]
Demence et VIH: neuropathologie.
Seilhean D; Duyckaerts C; Hauw J J
Laboratoire de Neuropathologie R. Escourolle, Hopital de la Salpetriere, Paris.
Journal of neuroradiology. Journal de neuroradiologie (FRANCE) Sep 1995, 22 (3) p161-2, ISSN 0150-9861 Journal Code: 7705086
Document type: Journal Article ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
? t s4/7/all

4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010373776 BIOSIS NO.: 199699007836
Regulation of lymphocyte homing into the brain during **viral** **encephalitis** at various stages of infection

AUTHOR: Irani David N (Reprint); Griffin Diana E
AUTHOR ADDRESS: Dep. Neurol., Johns Hopkins Hosp., Meyer 6-181, 600 N. Wolfe St., Baltimore, MD 21287-7681, USA**USA
JOURNAL: Journal of Immunology 156 (10): p3850-3857 1996 1996
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The passage of circulating lymphocytes into the central nervous system (CNS) during acute **viral encephalitis** was studied in vivo using fluorescently labeled cells inoculated into Sindbis virus (SV)-infected mice. Donor lymphocytes were detected in the brains of recipient animals when mononuclear cells were isolated from the CNS and screened by flow cytometry. The magnitude of this accumulation related to the duration of encephalitis in recipient mice and to the activation state of the inoculated cells. While Ag specificity did not influence lymphocyte entry into the inflamed CNS at any stage of infection, SV-immune cells were retained selectively within the brains of infected animals compared with cells of an irrelevant specificity. Coincident with the onset of CNS inflammation, ICAM-1 and VCAM-1 were up-regulated on cerebrovascular endothelium. Lymphocyte entry into the brains of infected animals during maximal inflammation could be inhibited by pretreating inoculated cells with Abs that blocked LFA-1, but not with those that blocked **VLA-4** or down-regulated CD44. None of these reagents prevented lymphocyte entry into the brain at the onset of inflammation, suggesting that the earliest recruited cells utilize presently uncharacterized receptor-ligand interactions. These data show that the degree of existing inflammation and the activation state of circulating cells, but not their Ag specificity, influence lymphocyte recruitment into the brain during SV encephalitis. While CNS homing can be blocked with Abs against known adhesion molecules during peak inflammation, lymphocyte entry into the brain during early infection remains poorly characterized.

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009655216 BIOSIS NO.: 199598123049
Immunopathogenic role of T-cell subsets in Borna disease **virus** -induced progressive **encephalitis**
AUTHOR: Planz Oliver; Bilzer Thomas; Stitz Lothar (Reprint)
AUTHOR ADDRESS: Inst. Virol., Justus-Liebig-Univ., Frankfurter Str. 107, D-35392 Giessen, Germany**Germany
JOURNAL: Journal of Virology 69 (2): p896-903 1995 1995
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Borna disease is an immunopathological virus-induced encephalopathy comprising severe inflammation and degenerative brain cell lesions which results in organ atrophy and chronic debility in rats. CD4+ and CD8+ T cells have been reported to be involved in the development of this disease of the central nervous system. A virus-specific homogeneous T-cell line, established in vitro after immunization of rats with the recombinant 24-kDa virus-specific protein, showed antigen-specific proliferation in the presence of the 24-kDa but not the 38-kDa Borna disease virus-specific protein, another major virus-specific antigen. This T-cell line, P205, was found to exhibit characteristics of a T-helper cell: CD4+ CD8- IL-2- IL-4- IFN-gamma+ IL-6+ IL-10+. Furthermore, this T-cell line expressed the alpha/beta T-cell receptor

and the alpha-4 integrin (**VLA-4**). Adoptive transfer of this helper cell resulted in an increase of antibody titers and two different types of disease in virus-infected rats after cyclophosphamide-induced immunosuppression. (i) Rats receiving T cells between 10 and 18 days after treatment with cyclophosphamide showed an acute lymphoproliferative disease in the gut and lungs within 9 days after adoptive transfer and died. (ii) Passive transfer within the first 5 days after immunosuppressive treatment resulted in typical Borna disease associated with neurological symptoms such as ataxia and paresis starting 14 to 16 days after transfer. Immunohistological analysis of the brains of rats with Borna disease uniformly revealed the presence of CD8+ T cells in encephalitic lesions in addition to CD4+ cells that were found in the brains of recipients of the virus-specific CD4+ T-cell line, irrespective of whether neurological symptoms developed or not. However, recipient rats treated with antibodies against CD8+ T cells developed neither encephalitis nor disease. Therefore, CD4+ T cells appear to accumulate in the brain and cause perivascular inflammatory lesions which alone obviously do not cause disease. In contrast, the presence of CD8+ cells apparently directly correlates with the development of neurological symptoms.

4/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008960032 BIOSIS NO.: 199396124448
A model of human immunodeficiency **virus encephalitis** in SCID mice
AUTHOR: Tyor William R (Reprint); Power Christopher; Gendelman Howard E; Markham Richard B
AUTHOR ADDRESS: Dep. Neurol., Med. Univ. South Carolina, 171 Ashley Ave., Charleston, SC 29425, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 90 (18): p8658-8662 1993
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Human immunodeficiency virus (HIV)-associated dementia complex is a common and devastating manifestation of the late phases of HIV infection. The pathogenesis of dementia complex is poorly understood and effective treatments have not been developed, in part because of the lack of an appropriate animal model. Mice with severe combined immunodeficiency (scid mice), which accept xenografts without rejection, were intracerebrally inoculated with human peripheral blood mononuclear cells and HIV. One to 4 weeks after inoculation, the brains of these mice contained human macrophages (some of which were HIV p24 antigen positive), occasional multinucleated cells, and striking gliosis by immunocytochemical staining. Human macrophages also were frequently positive for tumor necrosis factor type a and occasionally for interleukin 1 and **VLA-4**. Cultures of these brains for HIV were positive. Generally, human macrophages were not present in the brains of control mice, nor was significant gliosis, and HIV was not recovered from mice that received HIV only intracerebrally. Pathologically, this model of HIV encephalitis in scid mice resembles HIV encephalitis in humans and the data suggest that the activation of macrophages by infection with HIV results in their accumulation and persistence in brain and in the development of gliosis. This model of HIV encephalitis should provide insights into the pathogenesis and treatment of this disorder.

4/7/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05751151 EMBASE No: 1994154994
Monocyte adhesion to endothelium in Simian immunodeficiency **virus** -induced AIDS **encephalitis** is mediated by vascular cell adhesion molecule-1/alpha4beta1 integrin interactions
Sasseville V.G.; Newman W.; Brodie S.J.; Hesterberg P.; Pauley D.; Ringler D.J.
New England Reg. Primate Res. Center, Harvard Medical School, P.O. Box 9102,Southborough, MA 01772-9102 United States
American Journal of Pathology (AM. J. PATHOL.) (United States) 1994, 144/1 (27-40)
CODEN: AJPAA ISSN: 0002-9440
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Because the mechanisms associated with recruitment of monocytes to brain in AIDS encephalitis are unknown, we used tissues from rhesus monkeys infected with simian immunodeficiency virus (SIV) to examine the relative contributions of various adhesion pathways in mediating monocyte adhesion to endothelium from encephalitic brain. Using a modified Stamper and Woodruff tissue adhesion assay, we found that the human monocytic cell lines, THP-1 and U937, and the B cell line, Ramos, preferentially bound to brain vessels from monkeys with AIDS encephalitis. Using a combined tissue adhesion/immunohistochemistry approach, these cells only bound to vessels expressing vascular cell adhesion molecule-1 (VCAM-1). Furthermore, pretreatment of tissues with antibodies to VCAM-1 or cell lines with antibodies to **VLA-4** (CD49d) inhibited adhesion by more than 70%. Intercellular adhesion molecule-1 (ICAM-1)/beta2 integrin interactions were not significant in mediating cell adhesion to the vasculature in encephalitic simian brain using a cell line (JY) capable of binding rhesus monkey ICAM-1. In addition, selectin-mediated interactions did not significantly contribute to cell binding to encephalitic brain as there was no immunohistochemical expression of E-selectin and P-selectin in either normal or encephalitic brain, nor was there a demonstrable adhesive effect from L-selectin using L- selectin-transfected 300.19 cells on simian encephalitic brain. These results demonstrate that using the tissue adhesion assay, THP-1, U937, and Ramos cells bind to vessels in brain from animals with AIDS encephalitis using VCAM-1/alpha4beta1 integrin interactions and suggest that VCAM-1 and **VLA-4** may be integral for monocyte recruitment to the central nervous system during the development of AIDS encephalitis.

4/7/5 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11163639 98039725 PMID: 9372456
Semliki Forest virus infection leads to increased expression of adhesion molecules on splenic T-cells and on brain vascular endothelium.
Soilu-Hanninen M; Roytta M; Salmi A A; Salonen R
Turku Immunology Centre, University of Turku, Finland.
Journal of neurovirology (ENGLAND) Oct 1997, 3 (5) p350-60, ISSN 1355-0284 Journal Code: 9508123
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Semliki Forest virus A7 (SFV-A7) is a neurotropic alphavirus that leads to an asymptomatic encephalitis in adult immunocompetent mice. We studied the expression of leukocyte and endothelial cell adhesion molecules in the

spleen and in the central nervous system (CNS) during SFV-A7 infection. Kinetics of the expression of LFA-1 alpha/CD11a, LFA-1 beta/CD18, Mac-1/CD11b, **VLA-4**/CD49d, ICAM-1/CD54 and L-selectin/CD62L was determined on splenic CD4+ and CD8+ T-cells and macrophages by flow cytometry. Time course of the expression of these antigens and VCAM-1/CD106 as well as viral antigens in the CNS was studied by immunoperoxidase staining. In the spleen, a sustained increase in LFA-1-expression and a temporary increase at day 7 in the expression of **VLA-4**, Mac-1 and ICAM-1 were detected on CD8+ T-cells. L-selection was down-regulated on CD4+ cells. Adhesion molecules on macrophages remained unchanged. In the CNS, expression of Mac-1+, **VLA-4**+ and LFA-1+ cells increased in parallel with the kinetics of the expression of their ligands ICAM-1 and VCAM-1 on brain vessels. Upregulation of adhesion of molecules peaked between days 5-8 and was most prominent in the cerebellar and brain stem white matter where viral antigens were most abundant. We conclude that the adhesion molecules profile of splenic T cells is altered during SFV-A7 infection which may influence their homing into the CNS. Macrophages are probably recruited non-specifically as a consequence of activation of the brain vascular endothelium in the inflamed areas of the brain.

Record Date Created: 19971230
Record Date Completed: 19971230

4/7/6 (Item 2 from file: 155)

10241943 96043309 PMID: 7472530

[HIV and dementia: neuropathology]

Demence et VIH: neuropathologie.

Seilhean D; Duyckaerts C; Hauw J J

Laboratoire de Neuropathologie R. Escourolle, Hopital de la Salpetriere, Paris.

Journal of neuroradiology. Journal de neuroradiologie (FRANCE) Sep 1995 , 22 (3) p161-2, ISSN 0150-9861 Journal Code: 7705086

Document type: Journal Article ; English Abstract

Languages: FRENCH

Main Citation Owner: NLM

Record type: Completed

Cognitive disorders associated with HIV infection may be due to focal lesions (lymphoma, toxoplasmosis, progressive multifocal leukoencephalitis, etc.), metabolic encephalopathy (e.g. hepatic insufficiency) or psychiatric disorders (depression). In the absence of such causes a "cognitive and motor syndrome associated with HIV infection" has been defined on clinical criteria (Working group of the American Academy of Neurology, 1991). This syndrome is not consistently associated with any specific lesion. Neither the multifocal encephalitis of HIV or CMV infection nor the diffuse leukoencephalopathy associated with HIV are the only causes. The existence of a neocortical neuronal loss has been suggested by several retrospective studies, but our prospective study has not shown cortical or subcortical atrophy. Measurement of neuronal density in Brodmann's areas 4,9 and 40 has not revealed a significant loss either global, by layer, or by column. The only constant lesion was gliosis of the cortex and white matter. Neuronal loss, therefore, is not indispensable to the occurrence of cognitive disorders in AIDS. The mechanism of dementia might be: dysfunction of cortical neurons (dendritic abnormalities, virus/neurotransmitter competition); subcortical dysfunction, as suggested by the high density of microglial nodules in that region; white matter lesions which could be due to abnormalities in the blood-brain barrier. The expression of cell adhesion molecules (VCAM-1, **VLA-4** , ICAM-1 and LFA-1) by endothelial cerebral cells is not significantly different in AIDS patients, demented or not, and in patients with multiple sclerosis. In contrast, the expression of VCAM-1 by astrocytes is significantly increased in demented AIDS patients compared with non demented ones.(ABSTRACT TRUNCATED AT 250

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Phillips Gambel
ATU 164
11/20/03

0009655216 BIOSIS NO.: 199598123049
Immunopathogenic role of T-cell subsets in Borna disease virus -induced progressive encephalitis
AUTHOR: Planz Oliver; Bilzer Thomas; Stitz Lothar (Reprint)
AUTHOR ADDRESS: Inst. Virol., Justus-Liebig-Univ., Frankfurter Str. 107, D-35392 Giessen, Germany**Germany
JOURNAL: Journal of Virology 69 (2): p896-903 1995 1995
ISSN: 0022-538X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Borna disease is an immunopathological virus-induced encephalopathy comprising severe inflammation and degenerative brain cell lesions which results in organ atrophy and chronic debility in rats. CD4+ and CD8+ T cells have been reported to be involved in the development of this disease of the central nervous system. A virus-specific homogeneous T-cell line, established in vitro after immunization of rats with the recombinant 24-kDa virus-specific protein, showed antigen-specific proliferation in the presence of the 24-kDa but not the 38-kDa Borna disease virus-specific protein, another major virus-specific antigen. This T-cell line, P205, was found to exhibit characteristics of a T-helper cell: CD4+ CD8- IL-2- IL-4- IFN-gamma+ IL-6+ IL-10+. Furthermore, this T-cell line expressed the alpha/beta T-cell receptor and the alpha-4 integrin (VLA-4). Adoptive transfer of this helper cell resulted in an increase of antibody titers and two different types of disease in virus-infected rats after cyclophosphamide-induced immunosuppression. (i) Rats receiving T cells between 10 and 18 days after treatment with cyclophosphamide showed an acute lymphoproliferative disease in the gut and lungs within 9 days after adoptive transfer and died. (ii) Passive transfer within the first 5 days after immunosuppressive treatment resulted in typical Borna disease associated with neurological symptoms such as ataxia and paresis starting 14 to 16 days after transfer. Immunohistological analysis of the brains of rats with Borna disease uniformly revealed the presence of CD8+ T cells in encephalitic lesions in addition to CD4+ cells that were found in the brains of recipients of the virus-specific CD4+ T-cell line, irrespective of whether neurological symptoms developed or not. However, recipient rats treated with antibodies against CD8+ T cells developed neither encephalitis nor disease. Therefore, CD4+ T cells appear to accumulate in the brain and cause perivascular inflammatory lesions which alone obviously do not cause disease. In contrast, the presence of CD8+ cells apparently directly correlates with the development of neurological symptoms.

[Gambel, Phillip]
[Gambel, Phillip] _____

4/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008960032 BIOSIS NO.: 199396124448
A model of human immunodeficiency virus encephalitis in SCID mice
AUTHOR: Tyor William R (Reprint); Power Christopher; Gendelman Howard E; Markham Richard B
AUTHOR ADDRESS: Dep. Neurol., Med. Univ. South Carolina, 171 Ashley Ave., Charleston, SC 29425, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 90 (18): p8658-8662 1993
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Human immunodeficiency virus (HIV)-associated dementia complex is a common and devastating manifestation of the late phases of HIV infection. The pathogenesis of dementia complex is poorly understood and effective treatments have not been developed, in part because of the lack

MIC
QR180.36

STIC-ILL

From: Gambel, Phillip
Sent: Thursday, November 20, 2003 3:09 PM
To: STIC-ILL
Subject: viral encephalitis

stic

please provide the following references to

phillip gambel
art unit 1644
308-3997

1644 mailbox 9e12

4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010373776 BIOSIS NO.: 199699007836
Regulation of lymphocyte homing into the brain during viral encephalitis at various stages of infection
AUTHOR: Irani David N (Reprint); Griffin Diana E
AUTHOR ADDRESS: Dep. Neurol., Johns Hopkins Hosp., Meyer 6-181, 600 N. Wolfe St., Baltimore, MD 21287-7681, USA**USA
JOURNAL: Journal of Immunology 156 (10): p3850-3857 1996 1996
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The passage of circulating lymphocytes into the central nervous system (CNS) during acute viral encephalitis was studied in vivo using fluorescently labeled cells inoculated into Sindbis virus (SV)-infected mice. Donor lymphocytes were detected in the brains of recipient animals when mononuclear cells were isolated from the CNS and screened by flow cytometry. The magnitude of this accumulation related to the duration of encephalitis in recipient mice and to the activation state of the inoculated cells. While Ag specificity did not influence lymphocyte entry into the inflamed CNS at any stage of infection, SV-immune cells were retained selectively within the brains of infected animals compared with cells of an irrelevant specificity. Coincident with the onset of CNS inflammation, ICAM-1 and VCAM-1 were up-regulated on cerebrovascular endothelium. Lymphocyte entry into the brains of infected animals during maximal inflammation could be inhibited by pretreating inoculated cells with Abs that blocked LFA-1, but not with those that blocked VLA-4 or down-regulated CD44. None of these reagents prevented lymphocyte entry into the brain at the onset of inflammation, suggesting that the earliest recruited cells utilize presently uncharacterized receptor-ligand interactions. These data show that the degree of existing inflammation and the activation state of circulating cells, but not their Ag specificity, influence lymphocyte recruitment into the brain during SV encephalitis. While CNS homing can be blocked with Abs against known adhesion molecules during peak inflammation, lymphocyte entry into the brain during early infection remains poorly characterized.

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

of an appropriate animal model. Mice with severe combined immunodeficiency (scid mice), which accept xenografts without rejection, were intracerebrally inoculated with human peripheral blood mononuclear cells and HIV. One to 4 weeks after inoculation, the brains of these mice contained human macrophages (some of which were HIV p24 antigen positive), occasional multinucleated cells, and striking gliosis by immunocytochemical staining. Human macrophages also were frequently positive for tumor necrosis factor type a and occasionally for interleukin 1 and VLA-4. Cultures of these brains for HIV were positive. Generally, human macrophages were not present in the brains of control mice, nor was significant gliosis, and HIV was not recovered from mice that received HIV only intracerebrally. Pathologically, this model of HIV encephalitis in scid mice resembles HIV encephalitis in humans and the data suggest that the activation of macrophages by infection with HIV results in their accumulation and persistence in brain and in the development of gliosis. This model of HIV encephalitis should provide insights into the pathogenesis and treatment of this disorder.

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11/20/03

----------***[Gambel, Phillip]***

4/7/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05751151 EMBASE No: 1994154994
Monocyte adhesion to endothelium in Simian immunodeficiency virus -induced AIDS encephalitis is mediated by vascular cell adhesion molecule-1/alpha4beta1 integrin interactions
Sasseville V.G.; Newman W.; Brodie S.J.; Hesterberg P.; Pauley D.; Ringler D.J.
New England Reg. Primate Res. Center, Harvard Medical School, P.O. Box 9102,Southborough, MA 01772-9102 United States
American Journal of Pathology (AM. J. PATHOL.) (United States) 1994, 144/1 (27-40)
CODEN: AJPAA ISSN: 0002-9440
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Because the mechanisms associated with recruitment of monocytes to brain in AIDS encephalitis are unknown, we used tissues from rhesus monkeys infected with simian immunodeficiency virus (SIV) to examine the relative contributions of various adhesion pathways in mediating monocyte adhesion to endothelium from encephalitic brain. Using a modified Stamper and Woodruff tissue adhesion assay, we found that the human monocytic cell lines, THP-1 and U937, and the B cell line, Ramos, preferentially bound to brain vessels from monkeys with AIDS encephalitis. Using a combined tissue adhesion/immunohistochemistry approach, these cells only bound to vessels expressing vascular cell adhesion molecule-1 (VCAM-1). Furthermore, pretreatment of tissues with antibodies to VCAM-1 or cell lines with antibodies to VLA-4 (CD49d) inhibited adhesion by more than 70%. Intercellular adhesion molecule-1 (ICAM-1)/beta2 integrin interactions were not significant in mediating cell adhesion to the vasculature in encephalitic simian brain using a cell line (JY) capable of binding rhesus monkey ICAM-1. In addition, selectin-mediated interactions did not significantly contribute to cell binding to encephalitic brain as there was no immunohistochemical expression of E-selectin and P-selectin in either normal or encephalitic brain, nor was there a demonstrable adhesive effect from L-selectin using L- selectin-transfected 300.19 cells on simian encephalitic brain. These results demonstrate that using the tissue adhesion assay, THP-1, U937, and Ramos cells bind to vessels in brain from animals with AIDS encephalitis using VCAM-1/alpha4beta1 integrin interactions and suggest that VCAM-1 and VLA-4 may be integral for monocyte recruitment to the central nervous system during the development of AIDS encephalitis.

4/7/5 (Item 1 from file: 155
[Gambel, Phillip]

4732776 NO

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11/20/03

DIALOG(R)File 155:MEDLINE(R)

11163639 98039725 PMID: 9372456
Semliki Forest virus infection leads to increased expression of adhesion molecules on splenic T-cells and on brain vascular endothelium.
Soilu-Hanninen M; Roytta M; Salmi A A; Salonen R
Turku Immunology Centre, University of Turku, Finland.
Journal of neurovirology (ENGLAND) Oct 1997, 3 (5) p350-60, ISSN 1355-0284 Journal Code: 9508123
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Semliki Forest virus A7 (SFV-A7) is a neurotropic alphavirus that leads to an asymptomatic encephalitis in adult immunocompetent mice. We studied the expression of leukocyte and endothelial cell adhesion molecules in the spleen and in the central nervous system (CNS) during SFV-A7 infection. Kinetics of the expression of LFA-1 alpha/CD11a, LFA-1 beta/CD18, Mac-1/CD11b, VLA-4/CD49d, ICAM-1/CD54 and L-selectin/CD62L was determined on splenic CD4+ and CD8+ T-cells and macrophages by flow cytometry. Time course of the expression of these antigens and VCAM-1/CD106 as well as viral antigens in the CNS was studied by immunoperoxidase staining. In the spleen, a sustained increase in LFA-1-expression and a temporary increase at day 7 in the expression of VLA-4, Mac-1 and ICAM-1 were detected on CD8+ T-cells. L-selection was down-regulated on CD4+ cells. Adhesion molecules on macrophages remained unchanged. In the CNS, expression of Mac-1+, VLA-4+ and LFA-1+ cells increased in parallel with the kinetics of the expression of their ligands ICAM-1 and VCAM-1 on brain vessels. Upregulation of adhesion of molecules peaked between days 5-8 and was most prominent in the cerebellar and brain stem white matter where viral antigens were most abundant. We conclude that the adhesion molecules profile of splenic T cells is altered during SFV-A7 infection which may influence their homing into the CNS. Macrophages are probably recruited non-specifically as a consequence of activation of the brain vascular endothelium in the inflamed areas of the brain.
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6/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009866082 BIOSIS NO.: 199598333915
Immunopathogenesis of inflammatory myopathies
AUTHOR: Dalakas Marinos C
AUTHOR ADDRESS: Med. Neurol. Branch, NINDS, NIH, Build. 10, Room 4N248, 10 Center Drive MSC 1382, Bethesda, MD 20892-1382, USA**USA
JOURNAL: Annals of Neurology 37 (SUPPL. 1): pS74-S86 1995 1995
ISSN: 0364-5134
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Immune-mediated mechanisms appear to play a primary role in the pathogenesis of polymyositis (PM) and dermatomyositis (DM). The serum of patients with active DM has high levels of circulating complement fragments C3b, C4b, and C5b-9 membranolytic attack complex (MAC) and demonstrates a very high C3 uptake in an vivo assay system. The MAC and the immune complex-specific C3bNEO fragment are deposited on the endomysial capillaries early in the disease and lead sequentially to loss of capillaries, muscle ischemia, muscle fiber necrosis, and perifascicular atrophy. In contrast, in PM the muscle fiber injury is initiated by sensitized CD8+ cytotoxic T cells that recognize heretofore unknown and probably endogenous muscle antigens in the context of major histocompatibility complex (MHC) class I expression. A restricted (oligoclonal) pattern of T-cell receptor with prominence of Val, Vb6, and Vb15 genes is noted within the endomysial infiltrates suggesting that the T-cell response is antigen driven. In both PM and DM, intercellular adhesion molecule (ICAM)-1 and vascular cell adhesion molecule (VCAM)-1 are upregulated in the endomysial endothelial cells and function as ligands for the leukocyte integrins leukocyte function-associated antigen (LFA)-1 and very late activating antigen (VLA)-4, allowing activated lymphocytes to adhere to the endothelial cells and migrate to the muscle fibers. Among viruses, only the retroviruses human immunodeficiency virus (HIV) and human T-cell lymphotropic virus (HTLV)-I have been convincingly shown to trigger PM, which is mediated by nonvital-specific, cytotoxic CD8+ cells. The treatment of inflammatory myopathies remains empirical. Many patients respond to steroids to some degree and for some period of time. Azathioprine, methotrexate, cyclosporine, cyclophosphamide, and plasmapheresis can be of mild to moderate benefit. High-dose intravenous immunoglobulin (IVIg) is a promising therapeutic modality for some patients resistant to therapies. In a controlled study, IVIg was effective in DM not only in improving the clinical symptoms but also in reversing the underlying immunopathology. The role of IVIg in PM and IBM is under study in control